Corrected formal drawings will be filed in a subsequent communication.

C. Sequence Rules

The sequence 5'-GAGATGCGTCGGTGGCTG-3' set forth on page 45, line 5 of the specification will be provided in computer readable format as a Sequence Listing in a subsequent communication. This Sequence Listing is not required for examination of the pending claims since the pending claims are directed to a method of analyzing any sample in an integrated microfluidic device regardless of any specific sequence.

D. Patentability over the Cited Art

In the Office Action of August 3, 2000, the Examiner rejected claims 80-83, 85-96, and 98-107 under 35 USC §102 as being anticipated by U.S. Patent 5,587,128 to Wilding et al., and in the alternative under 35 USC §103(a) as obvious over U.S. Patent 5,587,128 to Wilding et al. Applicants respectfully disagree with these rejections for the reasons stated below. The Examiner also rejected dependent claims 84 and 97 as obvious over Wilding et al '128 in view of Schuipelsky et. al. '297 and Fodor et al. '186. Applicants again respectfully disagree with these rejections.

Importantly, the present invention is directed to a method of analyzing a sample in an integrated microfluidic device. The method includes supplying the sample into a first chamber, moving the sample from the first chamber to a second chamber, receiving a signal output from a reader device and indicating a property of the sample. The first chamber is selected from the group consisting of a chamber adapted to perform a preparative reaction, an analysis reaction, sample acquisition, DNA extraction, amplification, IV transcription or labeling. The second chamber is selected from the group consisting of a chamber adapted to perform a preparative reaction, an analysis reaction, sample acquisition, DNA extraction, amplification, IV transcription or labeling. In U.S. Patent 5,587,128, Wilding does not disclose or suggest this invention.

When rejecting claims 80-83, 85-96, and 98-107, the Examiner stated: "Wilding et al. disclose a method of extracting and purifying DNA and subsequently performing an amplification reaction of the same followed by detection of the amplification product.

As can be seen in said columns, the reactions are performed in an apparatus that is comprised of at least two reaction chambers and that the sample is caused to move from one reaction chamber to another." Applicants respectfully disagree with this statement for the following reasons.

While it is true that Wilding teaches extraction, purification and a subsequent amplification reaction of the same, these are not performed in two separate chambers, according to the teaching of Wilding. While with hindsight the use of two separate chambers may look obvious, this was not obvious more than five years ago, at the effective filing date of this application. The rapid and wide spread growth of biosciences frequently makes inventions of yesterday look obvious today. In the description, for example in col. 12, Wilding mentions reaction chambers and flow channels of different sizes and cross-sections only generically without specificity.

Regarding the Examiner's specific rejections, in col. 20 through 24 Wilding describes analytical devices shown in Figs. 6 through 13. For example in connection with Fig. 7 (and similarly Fig. 10), Wilding teaches in col. 21, lines 51 – 59 as follows: "FIG. 7 shows a schematic plan view of a substrate 14 fabricated with a system of flow channels 40 connected via channel 20 to ports 16 and a reaction chamber comprising sections 22A and 22B. The presence of amplified polynucleotide product in a sample will influence the flow characteristics within the flow channels. The channels 40 in this embodiment are symmetrically disposed and have a progressively narrower diameter towards the center of the pattern." (emphasis ours) Importantly, sections of a (one) reaction chamber cannot be equated to two reaction chambers.

Regardless of the above issues, assuming that the teaching of Wilding makes the original claims obvious (which Applicants do not concede), Wilding does not disclose or even suggest the use of confocal microscopy in a reader device, as now claimed on in independent claims 80 and 93. Confocal microscopy is not even hinted by Wilding.

The present invention is applicable to numerous integrated microfluidic devices, where various reactions are performed in separate reaction chambers and the samples

are then analyzed by performing confocal microscopy using a reader device. This provides important advantages described in the pending application.

Furthermore, claims 106 and 107 have been amended to include moving the sample from the first chamber to the second chamber by employing a valve located in the channel between the first chamber and the second chamber. Wilding not only does not teach the use of two separate chambers, as originally claimed, Wilding also does not even hint about the use of a valve located in a channel.

Accordingly, independent claims 80, 93,106 and 107 are clearly patentable over the prior art cited by the Examiner. Dependent claims 81 - 92, 94 – 105, 108 and 108 include additional novel combination of features. Therefore, all pending claims are in condition for allowance and such action is respectfully requested.

Please charge the extension fee of $890.00 and apply any other charges or credits to the Deposit Account No. 01-0431.

Respectfully submitted,

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Ivan D. Zitkovsky